UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,273	06/19/2003	Susan J. Braunhut	08688-057001 / UML 02-06	6439

26161 7590 11/03/2006

FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
SCHUBERG, LAURA J	

ART UNIT	PAPER NUMBER
1657	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,273	BRAUNHUT ET AL.	
	Examiner	Art Unit	
	Laura Schuberg	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 18-46* is/are pending in the application.

4a) Of the above claim(s) *21-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15, 18-20 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/01/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Applicant's arguments with respect to claims 1-15, 18-20 and 46 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The term "sufficient" in claim 10 is a relative term which renders the claim indefinite. The term "sufficient" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The phrase "sufficient number of living cells" is indefinite because the amount of cells required to form an extracellular matrix substantially free of cells (as required by the claim limitations) is not defined by the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 10-12, 18-20 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Rieck et al (Experimental Cell Research 1995).

Amended claim 1 is now drawn to a method of generating a morphogen composition from an extracellular matrix, the method comprising: growing cells on a surface under conditions and for a time sufficient to enable the cells to form an extracellular matrix (ECM); removing living cells from the surface and leaving the ECM on the surface; stimulating the extracellular matrix to release morphogens into the fluid; and collecting the fluid to form a morphogen composition. Dependent claims are drawn to wherein the morphogens are growth factors or differentiating factors, wherein the morphogen composition comprises a plurality of morphogens, wherein the fluid comprises a biocompatible liquid or gel, and further comprises removing a sufficient number of living cells from the ECM to form an ECM substantially free of living cells.

Amended claim 11 is now drawn to a morphogen composition comprising a plurality of morphogens including at least a fibroblast growth factor, or a transforming growth factor beta (Applicant elected fibroblast growth factor), wherein the morphogens are released from a stimulated ECM by the process as described in claim 1. Dependent claims include a biocompatible fluid - which is a buffer or a gel, wherein the composition

is in lyophilized form, wherein the ECM is substantially cell free, wherein the ECM is stimulated by an electric potential, wherein the electric potential is negative.

Claim 46 is drawn to a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a morphogen composition of claim 11.

Rieck teaches a method of extracting fibroblastic growth factor 2 (FGF2) from an ECM by growing endothelial cells, dissolving the cell layer, exposing the subendothelial matrix, and extracting the FGF2 with either 2M NaCl or trypsin thus forming a morphogen composition with fibroblast growth factor and a biocompatible fluid.

Claim 11 is a product-by-process claim; claims 12-15, 18-20 and 46 depend from said claim. M.P.E.P. § 2113 reads, "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps."

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive

structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979).

Therefore, the steps described in claims 11 and 18-20 are not given patentable weight since they don't affect the structure of the final product.

Therefore, the product produced by the method of Rieck is deemed to be the same as the one in claims 11, 12, 18-20 and 46.

Rieck, therefore, anticipates Applicants invention as claimed.

Claims 11-13, 15, 18-20 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Adami (US 5,714,458).

Claims 11, 12, 18-20 and 46 are drawn to the morphogen composition as described above.

Claim 13 further includes wherein the fluid is a buffer.

Adami teaches a stable lyophilized formulation of a fibroblast growth factor (FGF) (abstract). The addition of a buffer is taught (column 4 line 65) as well as the addition of sodium carboxymethyl cellulose (page 2 line 66), which is interpreted as a pharmaceutically acceptable carrier.

This composition taught by Adami is deemed to be structurally the same as that claimed by Applicant and therefore, Adami anticipates Applicant's invention as claimed.

Claims 11-15, 18-20 and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Whitehouse (US 2002/0032153 A1).

Claims 11, 12, 13, 18-20 and 46 are drawn to the morphogen composition as described above.

Claim 14 further includes wherein the fluid is a gel. Claim 15 further includes wherein the composition is in lyophilized form.

Whitehouse teaches a pharmaceutical composition that comprises FGF-2 in lyophilized form (page 7 –8 para 49). Prior to administration to a patient, the lyophilized product is reconstituted with a compatible sterile buffer (page 8 para 49). Whitehouse also teaches wherein the pharmaceutically acceptable carrier used is generally known in the art and includes gelatin, buffers (page 4 para 29) and also hydrogels (page 5 para 33).

This composition taught by Whitehouse is deemed to be structurally the same as that claimed by Applicant and therefore, Whitehouse anticipates Applicant's invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rieck et al (Experimental Cell Research 1995) as applied to claims 1-5, 10-12, 18-20 and 46 above, and further in view of Koyama et al (Nature Biotechnology 1997) and Simpson et al (US 2002/0090725 A1).

Claim 6 is dependent upon claim 1. Claims 7-9 are dependent upon claim 6. Claim 6 further includes wherein stimulating the extracellular matrix (ECM) comprises applying an electric potential to the extracellular matrix. Claim 7 further includes wherein the electric potential cycles from negative voltage to a positive voltage and back to a negative voltage. Claim 8 further includes wherein the electric potential ranges from – 0.3 V to +0.3 V. Claim 9 further includes varying frequency, potential range, potential cycle shape, or potential cycle number of the electric potential to control release and activation of specific morphogens.

Rieck teaches the method of claim 1 as described above.

Rieck does not teach wherein stimulating the ECM comprises applying an electric potential to the ECM.

Koyama teaches that electrical stimulation markedly promoted the nerve growth factor (NGF) secretion from astroglial cells (page 165 column 1 lines 19-22).

Simpson teaches that an electrical field can stimulate movement or conformational changes in a matrix due to the movement of magnetically or electrically sensitive particles. Such movement can affect the release of compounds from an electroprocessed matrix. Simpson further teaches that altering the conformation of the matrix can increase or decrease the extent to which the material is favorable for compound release.

Therefore, one of ordinary skill in the art would have been motivated to use an electric potential to stimulate the secretion of growth factors in the ECM in the method of Rieck because Koyama teaches that electrical stimulation promotes growth factor secretion from cultured cells (which include an ECM) and also because Rieck shows that there is more than one way to extract growth factor from an extracellular matrix. The modulation of the electric potential to comprise varying frequency, potential range, potential cycle shape or potential cycle number would have been a matter of routine optimization for one of ordinary skill in the art. The artisan recognizing that the optimum electric potential cycle and voltage would produce the greatest amount of cell growth and growth factor secretion. One of ordinary skill in the art would have had a reasonable expectation of success because Simpson teaches that an electrical field can stimulate movement or conformational changes in a matrix due to the movement of magnetically or electrically sensitive particles.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura Schuberg whose telephone number is 571-272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leon B Lankford, Jr
Primary Examiner
Art Unit 1651

Laura Schuberg